least 2 in at least 1 knee. 13.6% had an osteophyte score of at least 2 and 4.6% joint space narrowing of at least 2. Tibio-femoral osteoarthritis was present in 35.9% of patients. The mean intake of vitamin D was 3.17 micrograms a day, which is well below the recommended daily intake. Vitamin D intake was negatively associated with tibia femoral K&L score (p=0.028) and osteophyte score (p=0.013) but not tibio-femoral joint space score (p=0.28). The correlations were stronger in females than males, although the difference was not statistically significant. There were no associations between vitamin D intake and patello-femoral joint space score. There was no association between supplementary vitamin D intake and any of the radiographic variables.
Conclusions: Low vitamin D intake is associated with an increase prevelance of radiographic osteoarthritis and this is particularly driven by osteophytosis. There is no association with patello-femoral disease. Further work exploring vitamin D intake and osteoarthritis is recommended.

A33

A SNP LOCATED DOWNSTREAM OF BMP5 IS ASSOCIATED WITH ALLELIC EXPRESSION IMBALANCE AT THE GENE AND WITH PRIMARY OSTEOARTHRITIS

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Purpose: We have previously observed that the bone morphogenetic protein 5 gene BMP5 demonstrates a high degree of differential allelic expression (DAE) in articular cartilage chondrocytes, implying the presence of polymorphism within cis-regulatory elements of the gene. Our hypothesis is that this polymorphism confers OA susceptibility. The aim of this study was to map the variants that correlate with DAE at BMP5 and to then test their association with OA in a case-control cohort.
Methods: We genotyped 41 haplotype-tagging SNPs within a 416 kb interval encompassing and flanking BMP5 in 23 OA patients for whom we had determined the allelic expression profile. DAE status and SNP genotype were then correlated using the nonparametric Mann-Whitney test. Overall levels of BMP5 expression in chondrocytes were determined using real-time (RT)-PCR. Association analysis was performed on a cohort of 605 females with primary hip OA and 730 female controls, all of UK Caucasian origin. Ethical approval was obtained from local ethics committees.
Results: A SNP located 5kb downstream of BMP5 demonstrated significant correlation with DAE status ($P < 0.005$). The minor allele of the SNP was also correlated with an overall reduction in BMP5 expression as assessed by RT-PCR ($P = 0.03$). Homozygotes for the minor allele were significantly more prevalent in our cases (5.5%) than our controls (2.1%) with a P-value of 0.002 and odds ratio of 2.7 (95% CI 1.5-5.1). A subsequent detailed analysis of the HapMap revealed that the associated SNP is part of an extended haplotype block up to 80kb in length.
Conclusions: We have generated both genetic and functional data that support a role for downstream cis-acting regulatory elements of BMP5 as OA susceptibility loci.
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RISK PREDICTION OF KNEE OSTEOARTHRITIS USING MULTIPLE GENES

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Purpose: Primary osteoarthritis (OA) is the most common cause of joint disability in the developed world. A number of phenotypic risk factors have been identified and genetic factors are also major determinants of disease. The objective of this study was to assess how much of the risk of knee OA could be predicted by combinations of genetic polymorphisms associated in other populations with hip and/or knee OA.
Methods: Genetic polymorphisms in OA candidate genes were genotyped in 298 men and 305 women aged 50-86 diagnosed with knee OA assessed clinically and radiographically, and in 300 male and 299 female age and ethnicity matched controls. 18 OA candidate genes which had been previously reported to influence knee or hip OA risk or both were studied: *FRZB, COMP, COL2A1, VDR, AACT, ADAM12, CILP, BMP2, LRCH1, ESR1, OPG, TNA, COX2, CD36, NCOR2, TNFAIP6,ASPN, CALM1*. Genotype frequencies at a total of 37 polymorphisms in the above genes were compared between cases and controls separately by gender. We fitted a multivariate model with estimated knee OA risk as a function of all the polymorphisms in genes which were involved in this population as well as in independent studies. A new "OA genetic risk" variable was derived using the best fit in women with a minimum value of 0 and a maximum of 6. This same model was then tested in men.
Results: We found that SNPs in 12 genes were significantly associated with disease susceptibility in women in our cohort and SNPs in 8 of the genes were associated in men. The proportion of individuals affected with knee OA in the case-control study indicated that a much higher prediction of OA risk can be achieved by combining several genes which have consistently shown to be involved in OA genetic susceptibility. In particular we found that comparing women with a high "OA genetic risk" (>4) to those with low genetic risk (<2.5) resulted in an odds ratio of 11.15 (95%CI 5.1, 24.6$p < 1 \times 10^{-16}$). In men the same comparison resulted in OR= 4.27 (95%CI 2.4, 7.7 $p < 1 \times 10^{-7}$).
Conclusions: These data indicate that using a multiple gene approach, a higher genetic risk prediction is achievable in women with OA.

A35

RECOMIBINANT HUMAN CARTILAGE-DERIVED RETINOIC ACID SENSITIVE PROTEIN (CD-RAP) - A NOVEL TREATMENT OPTION FOR OSTEOARTHRITIS

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Purpose: Osteoarthritis is a significant worldwide health problem owing to the progressive and debilitating nature of the condition, which results in high morbidity and a marked decrease in the quality of life. It is the most common articular disorder in humans. New treatment options for this disease are required because currently no consistently working treatments are available.
Cartilage-derived retinoic acid sensitive protein (CD-RAP) is a highly specific marker for chondroid differentiation and has been shown in *in vitro* and *in vivo* assays to be a crucial determinant in cartilage differentiation and maintenance. It was evaluated whether CD-RAP alleviates or prevents cartilage degradation in an animal model of osteoarthritis.